27 MAY 2021 POSITIVE PHASE 1 RESULTS WITH IMMUNOTHERAPIES TARGETING PCSK9 TO TREAT HYPERCHOLESTEROLEMIA PUBLISHED BY THE EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY

- **Repeated immunisation with AFFITOPE® peptide active immunotherapy candidates AT04A and AT06A is safe, well-tolerated and induces a strong and long-lasting PCSK9-specific immune response**
- **AT04A treatment leads to significant LDLc-lowering activity of up to 39% in highest antibody responders**
- **Results further emphasise the value of the AFFITOPE® technology platform for potential first-in-class immunotherapies against a range of chronic non-communicable disease indications**

Vienna, Austria, May 27, 2021 – AFFiRiS AG, a clinical-stage biotechnology company developing novel disease-modifying Specific Active Immunotherapies (SAITs), today announced that detailed results of a large phase 1 clinical study with two of its AFFITOPE® peptide vaccine candidates in the cardiovascular disease indication hypercholesterolemia were published in the peer-reviewed journal European Journal of Clinical Pharmacology (https://doi.org/10.1007/s00228-021-03149-2). The results of the phase 1 trial demonstrated that repeated immunization with AT04A or AT06A is well tolerated, safe and elicited a humoral immune response against the PCSK9 target epitope. The data also showed that immunization with AT04A resulted in a significant reduction of low-density lipoprotein cholesterol (LDLc), with a reduction of up to 39% in the highest antibody responders.

One major risk factor for the development of atherosclerotic plaques, which can cause cardiovascular events such as heart attacks, is an increased level of LDLc. A pathway to reduce these risks involves targeting PCSK9 (proprotein convertase subtilisin/kexin type 9), a protein which downregulates the LDL receptor and therefore reduces uptake of LDLc. Neutralizing PCSK9 by induction of specific antibodies, results in reduced LDLc levels via an increased density of the LDL receptor.

In the single-blind, randomized, placebo-controlled trial, 72 healthy subjects were randomized to receive three priming immunizations at weeks 0, 4, and 8, and one booster immunization at week 60 of either AT04A, AT06A, or placebo. Participants were evaluated over a period of 90 weeks to assess safety, immunogenicity, and LDLc-lowering activity of both SAIT products targeting PCSK9.

The results of this large phase 1 trial demonstrated that active immunization with both AT04A and AT06A is safe and well-tolerated with no treatment-related severe adverse events (SAEs). No subjects discontinued due to treatment-

emergent adverse events (TEAEs). The most common related systemic TEAEs reported were fatigue, headache, and myalgia (75% in the AT06A group, 58% in the placebo group, 46% in the AT04A group) with the majority of events being mild. Injection-site reactions, which accounted for 63% of all TEAEs were transient and mostly of mild or moderate intensity. Both SAIT candidates induced a robust, long-lasting and boostable IgG antibody response towards the PCSK9 target epitope. Moreover, treatment with AT04A induced a group mean peak reduction in serum LDLc of 11.2% and 13.3% at weeks 20 and 70, respectively, when compared to placebo, with a maximal individual LDLc decrease of 39% at week 90 in the highest antibody responders.

“The safety profile and strong and sustained immune response elicited by the two peptide vaccine candidates AT04A and AT06A against the PCSK9 target epitope and in particular the LDLc-lowering activity of AT04A are encouraging results, supporting further development of the AT04 candidate”, said **Markus Zeitlinger, M.D., Associate Professor at the Medical University of Vienna and principal investigator of the study**.

“We are particularly excited to see that treatment with AT04A leads to a significant reduction in LDLc, which is a major risk factor for the development of atherosclerotic plaques. These findings are also in line with data from our preclinical studies that showed a significant decrease in atherosclerosis development after active immunization with AT04A.”, commented **Günther Staffler, PhD, Chief Technology Officer of AFFiRiS AG**. “These findings warrant selecting AT04 based immunotherapy for further clinical development in hypercholesterolemia and atherosclerosis.”

“The results of the trial now demonstrate the value of our specific active immunization approach in a cardiovascular indication”, added **Noel Barrett, PhD, CEO of AFFiRiS AG. “**This adds to the highly positive data obtained in a number of preclinical and clinical studies for chronic neurodegenerative disease indications and emphasizes the value of the AFFITOPE® technology platform for the immunotherapy of a variety of other chronic disease indications. Importantly, the demonstrated boostable antibody response demonstrated in this and other studies could pave the way for more patient-friendly therapeutic schedules and also circumvent high treatment costs by the stimulation of a self-produced, long-lasting immune reaction in indications with high medical need.”

About AFFITOPE’s® AT04A and AT06A:

Using its AFFITOME technology, AFFiRiS develops amino acid sequences that mimic the epitopes of self-proteins, which are modified by mutating the original amino acid sequence. These amino acid sequences, termed AFFITOPEs®, are coupled to a carrier protein and are formulated with an adjuvant to further enhance the immune response. The AFFITOPE® formulation, the basis of SAIT,

is administered to patients via a subcutaneous injection, which stimulates the generation of antibodies against the target proteins. AFFITOPE® AT04A and AT06A are AFFiRiS' novel immunotherapy candidates for the treatment of hypercholesterolemia. AT04A and AT06A consist of 10 amino acid long peptide variants of the epitope PCSK9 aa 153–162, coupled to a carrier protein and adjuvanted with aluminum hydroxide (Alhydrogel® – 0.5 mg aluminum equivalent per dose) in phosphate-buffered saline (PBS).

About AFFiRiS AG:

AFFiRiS is a clinical-stage biotechnology company located in Vienna, Austria, with a vision of using the immune system to identify and target human proteins central to the development and progression of neurodegenerative diseases, based on its proprietary patented AFFITOME® technology. The Company's ultimate goal is to improve the lives of patients suffering from these diseases by providing disease-modifying specific immunotherapies. With its lead candidate, AFFITOPE® PD01, AFFiRiS is the leader in active immunotherapies for Parkinson's disease. For further information, please visit www.affiris.com and follow us on LinkedIn and Twitter.

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About SAIT:
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